

In the Claims:

Please cancel claims 2, 4, 6, 7, 9, 11, 12, 14, 16-20, 22, and 25.

Please amend claims 1, 3, 5, 8, 10, 13, 15, 21, 23, 24, and 26.

Please add new claims 28-30.

No new matter has been added.

1. (currently amended) A ~~nonhuman~~ transgenic ~~animal~~ mouse comprising a modified glycoprotein V (GP V) gene, wherein said gene has been modified so that the ~~animal~~ mouse does not express a functional GP V protein or expresses a GPV protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein.

2. (canceled)

3. (currently amended) Platelets isolated from blood plasma of the ~~animal~~ mouse of any of claims 1 or 2.

4. (canceled)

5. (currently amended) A method of preparing a ~~nonhuman~~, transgenic ~~mammal~~ mouse comprising a modified glycoprotein V gene, wherein said gene has been modified so that the ~~mammal~~ mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein, said method comprising:

a) introducing into embryonic stem cells a nucleic acid molecule encoding a modified GP V gene; and

b) generating a transgenic ~~nonhuman-mammal~~ mouse from the cells resulting from step a).

6. (canceled)

7. (canceled)

8. (currently amended) The method of claim 5 further comprising the step of breeding the transgenic ~~nonhuman-mammal~~ mouse so as to produce a ~~nonhuman-mammal~~ mouse homozygotic for the modified GP V gene.

9. (canceled)

10. (currently amended) A method of preparing a ~~nonhuman~~, transgenic ~~mammal~~ mouse comprising a nonfunctional glycoprotein V gene, wherein said gene has been modified so that the ~~mammal~~ mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein, said method comprising:

- a) introducing into embryonic stem cells a nucleic acid molecule encoding a disrupted or nonfunctional GP V gene and a selectable marker;
- b) identifying and selecting transformed cells;
- c) injecting the transformed cells from step b) into blastocysts; and,
- d) generating a ~~nonhuman~~ transgenic ~~mammal~~ mouse from the blastocysts of step c), wherein the generated ~~nonhuman~~ transgenic ~~mammal~~ mouse is chimeric for the disrupted or nonfunctional GP V gene.

11. (canceled)

12. (canceled)

13. (currently amended) The method of claim 10 further comprising the following steps:

- e) breeding the chimeric ~~nonhuman-mammal~~ mouse with a wild-type ~~nonhuman~~ ~~mammal~~ mouse to produce a ~~nonhuman-mammal~~ mouse heterozygotic for the nonfunctional GP V gene;
- f) crossing a heterozygotic ~~nonhuman-mammal~~ mouse produced in step e) with a chimeric ~~non-human-mammal~~ mouse or a heterozygotic ~~nonhuman-mammal~~ mouse; and,
- g) selecting a ~~nonhuman-mammal~~ mouse homozygotic for the nonfunctional GP V gene from the resulting progeny.

14. (canceled)

15. (currently amended) A method to identify an agent that modulates a ~~biological~~ thrombotic response of a ~~nonhuman~~ transgenic ~~mammal~~ mouse having a modified GP V gene, wherein said gene has been modified so that the ~~mammal~~ mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced

functionality as compared with the native or wild-type GP V protein, comprising the step of exposing the ~~mammal~~ mouse to the agent and determining whether the agent modulates the thrombotic response.

16 - 20 (canceled)

21. (currently amended) A method of determining the effect of an agent on a characteristic of ~~an animal~~ a mouse that is attributable to the expression of the GP V gene, wherein said gene has been modified so that the ~~mammal~~ mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein, and wherein said characteristic is platelet function, said method comprising;

- C 4
- a) administering said agent to the ~~animal~~ mouse of claim 1;
  - b) maintaining said ~~animal~~ mouse for a desired period of time after said administration; and,
  - c) determining whether a ~~the~~ characteristic of said ~~animal~~ mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

22. (canceled)

23. (currently amended) A cell line isolated from a ~~nonhuman~~ transgenic ~~mammal~~ mouse that comprises a transgene stably integrated into the ~~mammal's~~ mouse's genome, said transgene encoding a modified glycoprotein V gene, wherein said gene has been modified so that the ~~mammal~~ mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein.

24. (currently amended) The cell line of claim 23, wherein said transgene has been introduced into said ~~nonhuman-mammal~~ mouse or an ancestor of said ~~nonhuman~~ ~~mammal~~ mouse via homologous recombination in embryonic stem cells, and further wherein said ~~nonhuman-mammal~~ mouse expresses a modified GP V protein.

25. (canceled)

26. (currently amended) The cell line of claim 25 24, wherein said mouse is fertile and transmits the modified GP V gene to its offspring.

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27. (original) The cell line of claim 23, wherein the modified GP V protein is nonfunctional.

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28. (new) A method of determining the effect of an agent on a characteristic of a mouse that is attributable to the expression of the GP V gene, wherein said gene has been modified so that the mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein, and wherein said characteristic is hemostasis, said method comprising;

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- a) administering said agent to the mouse of claim 1;
  - b) maintaining said mouse for a desired period of time after said administration; and,
  - c) determining whether the characteristic of said mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

29. (new) A method of determining the effect of an agent on a characteristic of a mouse that is attributable to the expression of the GP V gene, wherein said gene has been modified so that the mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein, and wherein said characteristic is coagulation, said method comprising;

- a) administering said agent to the mouse of claim 1;
- b) maintaining said mouse for a desired period of time after said administration; and,
- c) determining whether the characteristic of said mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.

30. (new) A method of determining the effect of an agent on a characteristic of a mouse that is attributable to the expression of the GP V gene, wherein said gene has been

modified so that the mouse does not express a functional GP V protein or expresses a GP V protein which demonstrates a reduced functionality as compared with the native or wild-type GP V protein, and wherein said characteristic is thrombosis, said method comprising;

- C<sup>1</sup>
- a) administering said agent to the mouse of claim 1;
  - b) maintaining said mouse for a desired period of time after said administration;  
and,
  - c) determining whether the characteristic of said mouse that is attributable to the expression of the modified GP V gene has been affected by the administration of said agent.
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